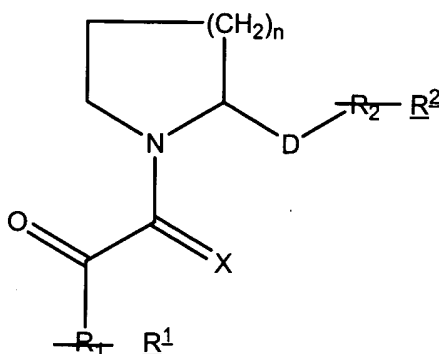


In the Claims:

In accordance with the Pre-OG Notice dated January 31, 2003 permitting amendments in a revised format, applicants provide the following listing of claims.

Claim 1 (currently amended): A compound ~~having the formula (I):~~ of formula



or a pharmaceutically acceptable salt, ester, or solvate of the compound, wherein:

n is 1-3;

X is either O or S;

~~R₁ R¹ is selected from the group consisting of~~ C₁-C₉ straight or branched chain alkyl, C₂-C₉ straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, ~~or a~~ C₁-C₁₀ straight or branched chain alkyl, C₂-C₁₀ alkenyl or C₂-C₁₀ alkynyl;

~~R₂ R² is a~~ carboxylic acid or a carboxylic acid isostere;

~~and wherein~~ said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from ~~R₃ R³~~ and Z, ~~where~~ ;

~~R₃ R³~~ and Z are independently hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C₁-C₆ straight

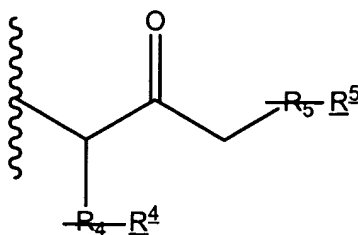
or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, or CO₂R⁷;

where R⁷ is hydrogen, or C₁-C₉ straight or branched chain alkyl or C₂-C₉ straight or branched chain alkenyl;

~~or a pharmaceutically acceptable salt, ester, or solvate thereof;~~

provided that ÷ when ~~n=1~~, and D is a bond, and ~~R₂~~ R² is COOH, then ~~R₄~~ R¹ is not C₁-C₉ straight or branched chain alkyl, C₂-C₉ straight or branched chain alkenyl, C₅-C₇ cycloalkyl, C₅-C₇ cycloalkenyl, phenylamine, 2-(3, 4-dichlorophenyl)ethyl, hydroxy, ethoxy, benzyl, or ~~Ar₄~~ Ar¹, wherein ~~Ar₄~~ Ar¹ is 1-naphthyl, 2-naphthyl, 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thiazolyl, 2-thienyl, 3-thienyl, 1-pyridyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, and wherein said alkyl, alkenyl, cycloalkyl, cycloalkenyl, or ~~Ar₄~~ Ar¹ ~~are is~~ optionally substituted with one or more substituents selected from the group consisting of ~~hydrogen~~, halo, hydroxyl, nitro, trifluoromethyl, C₁-C₉ straight or branched alkyl, C₂-C₉ straight or branched alkenyl, C₁-C₄ alkoxy, C₂-C₄ alkenyloxy, phenoxy, benzyloxy, COOH, and amino;

further provided that ÷ when ~~n=1~~, and D is a bond, and ~~R₂~~ R² is the carboxylic acid isostere -CONZ(R³), and Z is hydrogen or C₁-C₆ alkyl, and R³ is phenyl, or C₂-C₆ straight or branched chain alkyl or alkenyl, wherein said alkyl is unsubstituted or substituted in one or more positions with ~~Ar₂~~ Ar² as defined below, C₃-C₈ cycloalkyl, cycloalkyl connected by methyl or a C₂-C₆ straight or branched chain alkyl or alkenyl ~~chain~~, C₁-C₄ alkyl ester, or ~~Ar₃~~ Ar³ wherein ~~Ar₃~~ Ar³ is selected from the group consisting of 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thiazolyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, having one to three substituents independently selected from the group consisting of hydrogen, halo, hydroxy, nitro, trifluoromethyl, C₁-C₆ straight or branched alkyl, C₂-C₆ straight or branched alkenyl, C₁-C₄ alkoxy, C₂-C₄ alkenyloxy, phenoxy, benzyloxy, and amino; wherein said alkyl ester is optionally substituted with phenyl; or R³ is the fragment:



wherein R₄ R⁴ is selected from the group consisting of straight or branched chain C₁-C₈ alkyl optionally substituted with C₃-C₈ cycloalkyl, benzyl, or Ar₂ Ar² as defined below, and wherein R₂ R² is COOZ or CONR⁶, wherein R⁶ is selected from the group consisting of hydrogen, C₁-C₆ straight or branched alkyl, and C₂-C₆ straight or branched alkenyl, and wherein R₅ is selected from the group consisting of phenyl, benzyl, C₁-C₆ straight or branched alkyl, and C₂-C₆ straight or branched alkenyl, wherein said alkyl or alkenyl is optionally substituted with phenyl; then R₄ R¹ is not C₁-C₉ straight or branched chain alkyl, C₂-C₉ straight or branched chain alkenyl, substituted thiophene, or C₁-C₄ alkoxy, wherein said alkyl or alkenyl is optionally substituted in one or more positions with C₃-C₈ cycloalkyl, C₅-C₇ cycloalkenyl, or Ar₂ Ar² as ~~where Ar₂ is~~ defined below, wherein said alkyl, alkenyl, cycloalkyl or cycloalkenyl groups ~~may be~~ is optionally substituted with C₁-C₄ alkyl, ~~C₁-C₄~~ C₂-C₄ alkenyl, or hydroxy, and wherein Ar₂ Ar² is 1-naphthyl, 2-naphthyl, 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, having one to three substituents selected from the group consisting of hydrogen, halo, hydroxy, nitro, trifluoromethyl, C₁-C₆ straight or branched alkyl, C₂-C₆ straight or branched alkenyl, C₁-C₄ alkoxy, C₂-C₄ alkenyloxy, phenoxy, benzyloxy, and amino;

further provided that ÷ when ~~n=1, and~~ X is O, ~~and~~ D is a bond, and R₂ R² is -CONH₂, then R₄ R¹ is not methyl, ethyl, iso-propyl, iso-butyl, iso-pentyl, 4-methylpentyl, indolyl, phenyl, or hydroxyphenyl;

further provided that ÷ when ~~n=1, and~~ X is O, ~~and~~ D is a bond, and R₂ R² is cyano, then R₄ R¹ is not methyl;

~~further provided that:~~

~~when $n = 2$, and X is O , and D is a bond, and R_2 is $CONZ(R^3)$, and R_1 is ethoxy, then R^3 or Z is not halo-substituted phenyl;~~

~~further provided that:~~

~~when $n = 2$, and X is O , and D is a bond, and R_2 is $CONZ(R^3)$ and R_1 is substituted thiophene or tetrahydropyranoxy, or methoxy, then R^3 or Z is not C_1 - C_4 alkyl ester substituted ethyl;~~

~~further provided that:~~

~~when $n = 2$, and X is O , and D is a bond, and R_2 is $CONZ(R^3)$ and R_1 is ethoxy, then R^3 or Z is not 4-chlorophenyl;~~

~~further provided that:~~

~~when $n = 2$, and X is O , and D is a bond, and R_2 is $CONZ(R^3)$ and R_1 is cyclohexyl, then R^3 or Z is not ethyl or propyl substituted with phenyl;~~

further provided that : when D is CH_2 , then R_2 R^2 is not -OMe, -NHMe, or substituted -NHcyclohexyl; and

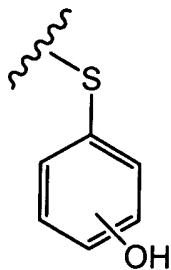
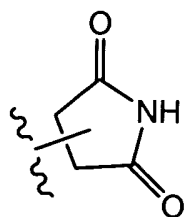
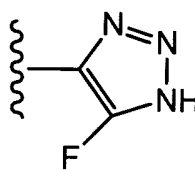
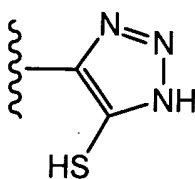
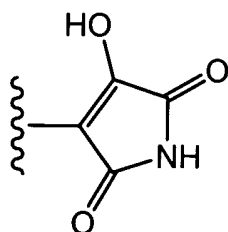
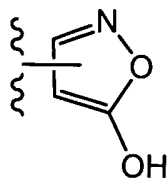
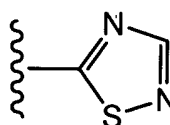
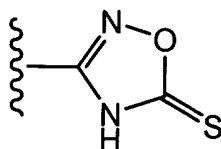
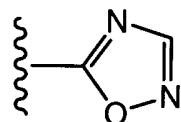
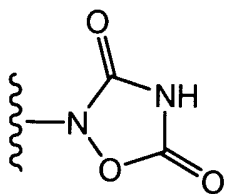
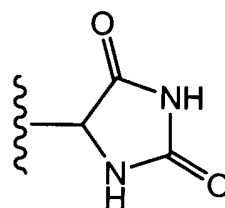
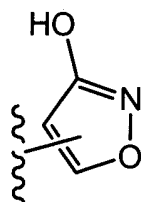
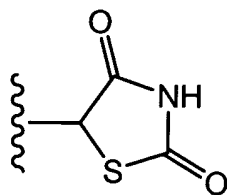
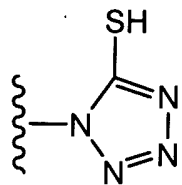
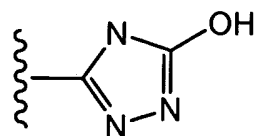
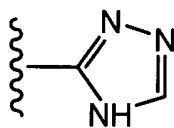
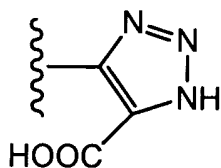
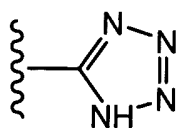
further provided that : when D is CH_2 , and R_2 R^2 is -OH, then R_1 R^1 is not phenyl or pyrrolidinemethanol ;

~~further provided that:~~

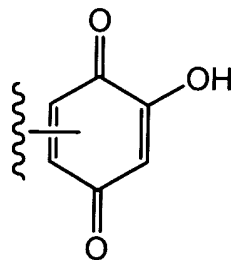
~~when $n = 2$, and X is O , and D is a bond, and R_2 is $COOH$, then R_1 is not methyl, tert butyl, 1,1 dimethyl 2 methyl propyl, 1,1 dimethyl propyl, methoxy, ethoxy, phenyl, tetrahydropyranoxy substituted C_4 - C_6 alkyl, 1 methyl 1 methoxyamide, 1-methylcyclohexyl, 3-iodophenyl, 3-methyl ester cyclopentyl, 1,1 dimethyl 6-phenyl-hex 3,5-dioxy, or trimethoxyphenyl.~~


Claim 2 (currently amended): The compound of claim 1, wherein R_2 R^2 is a carbocycle or heterocycle containing any combination of CH_2 , O , S , or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are is optionally substituted in one or more positions with R^3 .

Claim 3 (currently amended): The compound of claim 1, wherein R_2 R^2 is **selected from the group consisting of:**




or



 wherein the atoms of said ring structure ~~may be~~ is optionally substituted at one or more positions with R³.


Claim 4 (canceled)

 Claim 5 (currently amended): The compounds, (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-hydroxymethylpyrrolidine; (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinetetrazole; (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarbonitrile; ~~and (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-aminocarbonyl piperidine;~~ and compounds ~~1-25, 27, 28, 31-33, and 35-136~~ 1, 3, 5, 8, 11, 14, 17, 21, 24-32, 34, 38-40, 44, 45, 47-52, 62, 64-68, 73-98, 101, 102, 106, 108-117 and 119-137 of Tables I, II, and III.

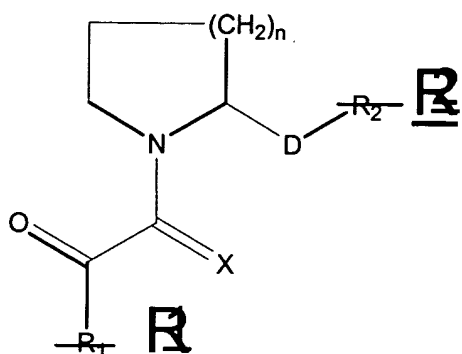
Claim 6 (original): The compound 1-{2-[3-(4-Fluorophenyl)(1,2,4-oxadiazol-5-yl)]pyrrolidinyl}-3,3-di-methylpentane-1,2-dione.

Claim 7 (original): The compound 3,3-Dimethyl-1-[2-(3-methyl(1,2,4-oxadiazol-5-yl))pyrrolidinyl]pentane-1, 2-dione.

Claim 8 (canceled)

 Claim 9 (currently amended): ~~The pharmaceutical composition of claim 8, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere comprises A~~ pharmaceutical composition comprising:

(i) a compound of formula (I) !



or a pharmaceutically acceptable salt, ester, or solvate of the compound, wherein:

n is 1-3;

X is either O or S;

R₁ is ~~selected from the group consisting of~~ C₁-C₉ straight or branched chain alkyl ~~or alkenyl~~, C₂-C₉ straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;

D is a bond, ~~or a~~ C₁-C₁₀ straight or branched chain alkyl, C₂-C₁₀ alkenyl or C₂-C₁₀ alkynyl;

R₂ **R²** is carboxylic acid or a carboxylic acid isostere;

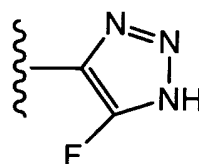
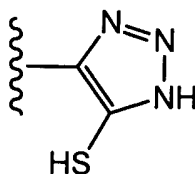
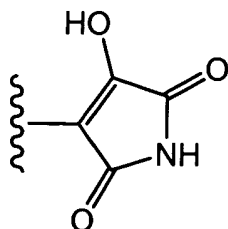
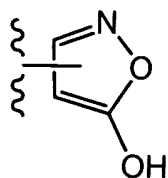
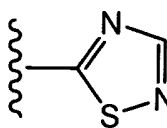
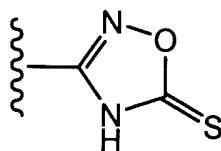
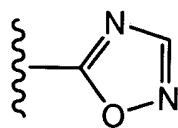
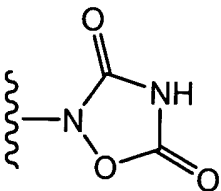
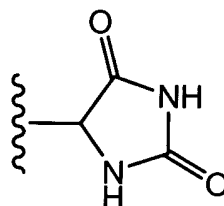
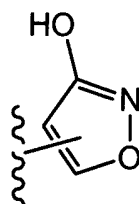
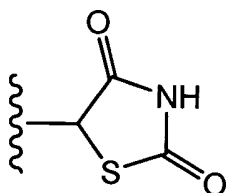
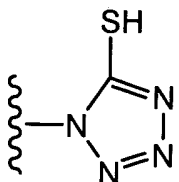
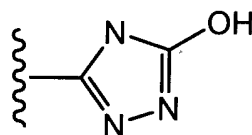
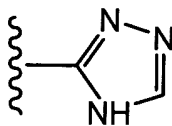
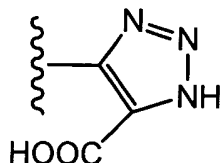
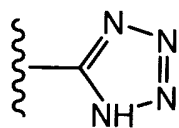
~~and wherein~~ said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is optionally substituted with one or more substituents selected from ~~R³, where R³ is hydrogen~~, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO₂R⁷ ~~wherein~~ R⁷ is hydrogen, ~~or~~ C₁-C₉ straight or branched chain alkyl or C₂-C₉ straight or branched chain alkenyl; and
~~or a pharmaceutically acceptable salt, ester, or solvate thereof~~

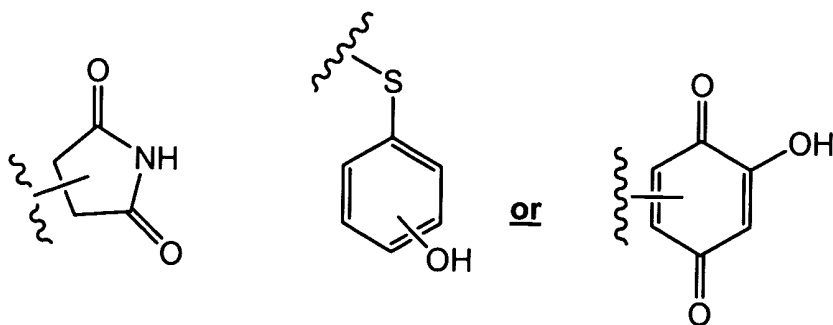
(ii) a pharmaceutically acceptable carrier.

Claim 10 (currently amended): The pharmaceutical composition of claim 9, wherein **R₂** **R²** is a carbocycle or heterocycle containing any combination of CH₂, O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure ~~are~~ is optionally substituted in one or more positions with R³.

Claim 11 (currently amended): The pharmaceutical composition of claim 9, wherein **R₂** **R²** is ~~selected from the following group:~~

B³
cont.





B³
cont. wherein the atoms of said ring structure ~~may be~~ is optionally substituted at one or more positions with R³.

Claim 12 (canceled)

B⁴
Claim 13 (currently amended): The pharmaceutical composition of claim 9, wherein the ~~N-heterocyclic carboxylic acid or carboxylic acid isostere~~ compound is selected from the group consisting of compounds ~~1-139~~ 1, 3, 5, 8, 11, 14, 17, 21, 24-32, 34, 38-40, 44, 45, 47-52, 62, 64-68, 73-98, 101, 102, 106, 108-117 and 119-137 of Tables I, II and III.

Claims 14-82 (canceled)